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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/719,311

11/20/2003

John A. Chiorini

14014.0252U3

3284

36339

7590

09/03/2009

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EXAMINER

BURKHART, MICHAEL D

ART UNIT

PAPER NUMBER

1633

MAIL DATE

DELIVERY MODE

09/03/2009

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/719,311	<b>Applicant(s)</b> CHIORINI ET AL.	
	<b>Examiner</b> Michael Burkhart	<b>Art Unit</b> 1633	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 04 June 2009.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 2,3,6-28,30-36 and 38-45 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 2, 3, 6-28, 31-36, and 38-45 is/are rejected.
- 7) ☒ Claim(s) 30 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

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### **DETAILED ACTION**

Receipt and entry of the amendment dated 6/4/2009 is acknowledged. After entry of the amendment, claims 2, 3, 6-28, 30-36, and 38-45 are pending and under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

#### ***Claim Rejections - 35 USC § 112***

Claims 2-3, 6-28, 31-36 and 38-45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods and compositions comprising the AAV4 proteins set forth in SEQ ID NOs: 2, 4, 8, 9, 10, 11, 16 and 18, does not reasonably provide enablement for the claimed variants thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Claims 2-3, 6-28, 30-36 and 38-45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

**These rejections are maintained for reasons made of record in the Office Actions dated 4/21/2006, 3/4/2009, and for reasons set forth below.**

#### ***Response to Arguments***

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Applicant's arguments filed 6/4/2009 have been fully considered but they are not persuasive. Applicants essentially assert that: 1) the Examiner has inappropriately combined arguments supporting Written Description and Enablement arguments; 2) the Examiner has misapplied the law because it is not necessary to provide a correlation between structure and function if applicants are relying upon structure; 3) the Written Description guidelines present an example wherein claiming 85% sequence identity to a known sequence would meet the Written Description requirement; 4) in setting forth the scope of the claimed genus in a mathematical form, the Examiner has inappropriately mixed the Written Description and Enablement requirements; 5) a claim limited to SEQ ID NO: 4 has little value to applicants; 6) the enablement rejection is based upon the breadth of the claims, and the inability of the skilled artisan to make  $3 \times 10^{192}$  variations of SEQ ID NO: 4, however, the skilled artisan would not attempt to make such a broad genus of variants; 7) the skilled artisan would only have to test a few variants to know whether or not the variants were functional; 8) the information in the art provides means to make variants above 70% homology, and the rejection has not provided any scientific or legal reasoning to refute this; 9) Rudinger et al is not a modern reference and does not speak to predicting functional variants; 10) the Ngo et al reference is misplaced; 11) the skilled artisan could have used knowledge in the prior art to identify conserved regions subject to predictable modification; 12) applicants request the Examiner to identify the level of homology that would be enabled.

Regarding 1), as explained in the previous Office Action, the combination of both rejections was due to the fact that the instant application fails to meet either requirement for

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essentially the same reasons. A review of the MPEP and the prosecution history reveals nothing inappropriate about rejecting the claims under both Written Description and Enablement. The reasons for doing so are extensive and of record.

Regarding 2), the application of the case law stands. Applicants attempt to interpret the applied case law to their advantage, asserting that the decisions spoke towards the skilled artisan not knowing what was actually being claimed as it was not disclosed. This is a problem covered under 35 USC 112-2nd ¶, not 35 USC 112-1st ¶. Rather than the Examiner, it is applicants who do not fully appreciate the statutes. Regarding Written Description, the case law indicates that applicants must show possession of the claimed scope, not whether or not the claimed scope was clear to the skilled artisan. It has been detailed how such possession can be demonstrated in an application, and why the instant application lacks such possession of the claimed genus. The fact remains applicants disclose the structure of a single species, SEQ ID NO: 4, and attempt to claim an extremely broad genus related to SEQ ID NO: 4 based upon nothing more than function. This is the exact situation outlined in the cited case law, i.e. the claimed structures were not known and could not be predicted, hence, possession of the genus did not exist.

Regarding 3), as previously set forth, the Guidelines are not rule making and are not binding. Therefore, it is not "factually and legally" correct to drop the Written Description requirement based on such guidelines. Such Guidelines do not take into account the reasoning set forth in the previous Office Action. Finally, it is noted that several claims do recite functions (e.g. claims 43-45).

Regarding 4), the Written Description requirement is essentially a genus/species comparison, wherein a single, or a number of, species are disclosed and it is to be determined if

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such a disclosure warrants possession of the claimed genus. Therefore it is unclear why applicant believes an analysis of the scope of the claimed genus is not useful in this instance. Merely naming a protein sequence that may or may not exist, or may or may not have the necessary function, is not in compliance with the provisions of 35 USC 112 1st ¶ for reasons of record.

Regarding 5), this is not a consideration in rejections under 35 USC 112-1st ¶.

Regarding 6) and 7), the analysis of the claimed scope stands, and thus the specification must teach how to make and use a scope that is commensurate with the claims. Merely finding one variant that is functional is not commensurate with the claimed scope of variants, and the skilled artisan could not determine *a priori* which variants would be functional or not. An almanac of all the possible variants is within the claimed scope for reasons of record, is not disputed, and includes, even at 99% homology,  $2.3 \times 10^{22}$  variants. The instant specification provides no guidance or working examples for how to create and test such a large number of variants, let alone such a process wherein the experimentation is undue. Applicants attempt to ignore this issue with hand-waving arguments that the skilled artisan could find some functional variants upon testing some. That is likely true, but does not address the heart of the issue, which is the claimed scope of variants and how to determine which, out of the  $3 \times 10^{19}$ , would be functional without undue experimentation.

Regarding 8), the cited reference (Tian et al) is from 2003, and cannot enable an application seeking a filing date of 1996. Tian et al does not teach how to determine functional variants for the instantly claimed protein, let alone the how to do so commensurate in scope with the claims. That functional variants exist within the claimed genus is stipulated, however, such

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variants are not disclosed by applicants or the prior art. Thus, the skilled artisan would have to discover them using tedious trial and error experimentation because such variants cannot be predicted.

Regarding 9) and 10), the teachings of Rudinger et al are as relevant today as in 1976. Protein structure and functionality cannot be predicted upon amino acid sequence alone. Applicants provide no reasoning or evidence to refute this. Rather, applicants make a vague assertion that Rudinger et al is not relevant to predicting functional variants, but rather the biological significance of amino acid changes to the activity of the peptide. This is nothing more than arguing semantics. Because applicants provide no methods to predict functional variants from the amino acid sequence of SEQ ID NO: 4, Ngo et al is relevant as a prior art method that attempts to do so by modeling. For reasons of record, it fails to accurately predict functional variants and thus does not enable the claims. Changes in tertiary structure of a protein do alter the function of proteins as exemplified by Rudinger et al. That some variants will not be functional is the very point of this rejection, as the breadth of the claims and the inability to predict non-functional variants without undue experimentation is the crux of this rejection.

Regarding 11), this is not disputed. However, the claims are not limited to substitutions or variants within the conserved regions, and for reason of record, even minor changes in conserved amino acids can abrogate protein function. It is impossible to tell beforehand what effects such substitutions or variations will have on the protein, hence the unpredictable nature of making and using such variants.

Regarding 12), claim 30 has been indicated as enabled. Preparing and testing up to two (2) amino acid substitutions within the claimed SEQ ID NO: 4 is also considered enabled.

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***Allowable Subject Matter***

Claim 30 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

***Conclusion***

No claims are allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Burkhart whose telephone number is (571)272-2915. The examiner can normally be reached on M-F 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael Burkhardt/  
Primary Examiner, Art Unit 1633